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EXAMINER	
MCKENZIE, THOMAS C	

ART UNIT	PAPER NUMBER
1624	

DATE MAILED: 04/29/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/067,017	MIGAWA ET AL.	
	Examiner	Art Unit	
	Thomas McKenzie Ph.D.	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) _____ is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. This action is in response to amendments filed on 3/8/04. Applicant has amended claims 2, 3, 11, 15, 19, 23, 27, 31, 35, 35-37, 39, 42, and 43. Applicant has canceled claim 1. Claim 44 is new.

Response to Amendment

2. Applicants' limitation of claim 44 to the elected subject matter overcomes the objection made in point #3 of the previous office action. Applicants' correction of some minor typos overcomes the objections made in points #4 and #5, as well as the indefiniteness rejection made in point #11. Applicants' addition of cycloalkyl overcomes the indefiniteness rejection made in point #7. Applicants replacement of "an ~alkyl(heteroyl)" by "heteroalkyl" overcomes the indefiniteness rejections made in points #8 and #9. The term "heteroalkyl" is used in the definition of R_5 in line 15, page 4 and does not introduce new matter. However, the meaning of heteroalkyl is discussed below. Applicants recitation of the leaving group N_3 to be used in their claimed process overcomes both the indefiniteness rejection made in point #10 and the enablement rejection made in point #14. Applicants' deletion of "prodrug" overcomes the indefiniteness rejections made in point #12 and #13 as well as the enablement rejection made in point #16. Applicants' limitation of R_2 to be a substituted amino group overcomes the art rejections over both Clark

(Antibiotica, Ref. 2) and Coutsogeorgopoulos (J. Med. Chem., Ref. 3) made in points #17 and #18.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 2-34 and 37-43 remain rejected and claim 44 is newly rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In claim 44, lines 7, 9, 11, 14, 15, 19, and 23, and in line 4, claim 2, Applicants claim "heteroalkyl" and "substituted heteroalkyl". In line 9, they like the term so much, they use it twice. In line 8, claim 44, they claim "alkyleneheteroalkyl". In line 10, claim 44 they claim, "heteroalkylenyl". What are these radicals? Nowhere in the specification are they defined. In the passage spanning line 24, page 7 to line 8, page 8, Applicants define "alkyl". Lines 23-25, page defines "heterocycloalkyl" but there is no definition of heteroalkyl. There is a second and conflicting definition of "alkyl" in lines 16-19, page 11. The word "heteroalkyl" is indefinite. There is no such thing. Is it an alkyl substituted by a heterocycle, e.g. pyridyl-methyl? An alkyl interrupted by a heteroatom, such as 2-ethoxyethyl? An alkyl substituted by a heteroatom, e.g. 2-chlorohexyl? Is "alkyleneheteroalkyl" an

alkylenehetero attached to an alkyl or an alkylene attached to a heteroalkyl? How does a "heteroalkyl" differ from a "heteroalkylenyl"? Are they the same? Whatever choice is selected must be supported by the specification.

The Examiner suggests deleting "heteroalkyl" and relying upon substituted alkyl, if that is what they intend.

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 42 remains rejected and claim 43 is newly rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating bacterial infections, does not reasonably provide enablement for "administering" the composition generally. The specification does not enable any physician skilled in the art of medicine, to make the invention commensurate in scope with these claims. The how to make requirement of the enablement statute, when applied to process claims, refers to operability and how to make the claimed process work. "The factors to be considered [in making an enablement rejection] have been summarized as the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in that art, the

predictability or unpredictability of the art and the breadth of the claims", *In re Rainer*, 146 USPQ 218 (1965); *In re Colianni*, 195 USPQ 150, *Ex parte Formal*, 230 USPQ 546. To whom is the composition to be given? Is everyone, well or sick to be given the composition?

a) Determining if any particular claimed compound would treat every human disease would require synthesis of the compound, formulation into a suitable dosage form, and subjecting it clinical trials with every different human disease, or to testing them in an assay known to be correlated to clinical efficacy of such treatment. This is a huge degree of experimentation. b) There is no direction concerning treating any diseases found in the specification. Applicants describe formulations in the passage spanning line 4, page 15 to line 2, line 30. There are no working examples of any formulation anywhere in this lengthy passage. Applicants do not teach the doses required to practice their invention anywhere in the specification. Since no compound has ever been used to treat every human disease, how is the skilled physician to know what dose to use for each of these different diseases? There is are *in vitro* assays drawn to 8 bacteria and 1 fungus species described in the passage spanning line 15, page 61 to the end of page 71. None of the tables of data are labeled with the microorganism used, so how is the physician to know which compound to use with which bacteria? A Table 3 is

mentioned but is missing from the specification. c) There is no working example of treatment of any disease in man or animals. d) The nature of the invention is clinical treatment of disease, which involves physiological activity. e) The state of the clinical arts is that no compound has ever been found that will "give a desired result" with every known disease.

f) The artisan using Applicants invention would be a physician with a MD degree and several years of experience. g) It is well established that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved", and physiological activity is generally considered to be an unpredictable factor. See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). h) The scope of the claims involves all of the thousands of compounds of claim 1 as well as the uncounted number of diseases embraced by the claim. Thus, the scope of claims is very broad.

MPEP §2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed.

Cir. 1993)." That conclusion is clearly justified here and undue experimentation will be required to practice Applicants' invention.

Applicants have removed the phrase "a desired result" from claim 42. Beyond broadening the scope of the claim to now include treating well people for whom no "desired result" is required, this not address the issue of the scope of medical treatment for which Applicants' are enabled.

Allowable Subject Matter

5. Claims 2-34, 37-41, and 44 would be allowable if rewritten or amended to overcome the rejection(s) under 35 U.S.C. 112, second paragraph, set forth in this Office action. Claims 35 and 36 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

6. Information regarding the status of an application should be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at (866) 217-9197 (toll-free). Please

direct general inquiries to the receptionist whose telephone number is (703) 308-1235.

7. Please direct any inquiry concerning this communication or earlier communications from the Examiner to Thomas C McKenzie, Ph. D. whose telephone number is (571) 272-0670. The FAX number for amendments is (703) 872-9306. The PTO presently encourages all applicants to communicate by FAX. The Examiner is available from 8:30 to 5:30, Monday through Friday. If attempts to reach the Examiner by telephone are unsuccessful, please contact James O. Wilson, acting SPE of Art Unit 1624, at (571)-272- 0661.

Thomas C. McKenzie, Ph.D.
Patent Examiner
Art Unit 1624

TCMcK/me